Remarks

Claims 4-6, 10-12 and 17-19 are pending. Claims 1-3, 7-9 and 13-16 have been canceled. Claims 4-6 and 17 have been withdrawn from consideration as being drawn to a non-elected invention.

Rejection Under 35 U.S.C. § 103

Claims 10-12 and 18 were rejected under 35 U.S.C. § 103(a) as being obvious over U.S. Patent No. 5,696,147 to Galardy ("Galardy"), Al Alousi et al. *J Cutan Pathol.* 23(6):506-510, 1996 ("AlAlousi") and Arbiser et al. *J Am Acad Dermatol.* 40(6 Pt 1):925-929, 1999 ("Arbiser 1999") in view of Thaloor et al. *Cell Growth Differ.* 9(4):305-12, 1998 ("Thaloor"). In addition, claims 10-12 and 19 were rejected under 35 U.S.C. § 103(a) as being obvious over Arbiser et al. *Mol Med.* 4(3):191-195, 1998 ("Arbiser 1998") in view of Thaloor. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

Claim 10 is drawn to the treatment of certain disorders with a curcuminoid. Claim 10 has been amended to recite recessive dystrophic epidermolysis bullosa in order to provide proper antecedent basis for language used in claim 19, and to delete angiosarcoma, hemangioendothelioma and Kaposi's sarcoma.

Galardy, Al Alousi, Arbiser 1998 and 1999

These references disclose diseases recited in the claims, angiosarcoma, hemangioendothelioma, Kaposi's sarcoma, malignant melanoma and recessive dystrophic epidermolyis bullosa (RDEB), but do not suggest the treatment of any of these disorders with a

curcuminoid. In addition, the Examiner alleges that these references disclose that the diseases are characterized by angiogenesis, which is defined as the growth of new blood vessels. Applicants submit that this is incorrect. Some of the references do not specifically state that the conditions are characterized by new blood vessel growth, they only attempt to demonstrate a relationship between bFGF and the disease.

For example, AlAlousi, which discloses cutaneous malignant melanoma (CMM), does not demonstrate that this disease is characterized by angiogenesis and in fact, teaches away from it. A study was reported by AlAlousi to determine if bFGF, an angiogenesis factor, plays a role in the evolution of CMM. The results of the study, which categorized CMM into (1) lesions that exhibited subsequent recurrence and (2) recurrence-free lesions, demonstrated that the expression of bFGF within the tumors and in peritumoral and intratumoral blood vessels was no different in the two groups. Furthermore, AlAlousi does not suggest that this disease is characterized by new blood vessel growth. The only way this reference attempts to link CMM to angiogenesis is through bFGF, and since it fails to show that bFGF affects the biological activity of CMM, it does not demonstrate that this disease is mediated by angiogenesis.

Arbiser 1998, which discloses recessive dystrophic epidermolysis bullosa (RDEB), demonstrates that bFGF is elevated in patients with this disease. The reference suggests that the increase of bFGF may contribute to increased fibroblast collagenase and the development of squamous cell carcinoma, but does not say that it contributes to the growth of new blood vessels.

Therefore, the disclosure of Arbiser 1998 does not demonstrate a clear link between RDEB and angiogenesis.

The diseases disclosed in Galardy and Arbiser 1999, angiosarcoma, Kaposi's sarcoma and hemangioendothelioma, have been deleted from the claims.

Thaloor

Thaloor et al. teaches the inhibition by curcumin of HUVEC growth and formation of tube structures on Matrigel, in a model of capillary formation. Their findings suggest that curcumin modulates protease activity during endothelial morphogenesis. The results of the study are limited to *in vitro* assays and do not suggest the administration of a curcuminoid to a patient or treatment of the specific diseases recited in the claims.

The Combination of Thaloor with Al Alousi, and Arbiser 1998 and 1999

None of the references alone or in combination teach or suggest the treatment of malignant melanoma or recessive dystrophic epidermolysis bullosa by administering a curcuminoid to a patient in order to inhibit angiogenesis.

Allowance of claims 10-12, 18 and 19 is respectfully solicited.

Respectfully submitted,

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Certificate of Facsimile Transmission

I hereby certify that this Amendment and Response to Office Action, and any documents referred to as attached therein are being facsimile transmitted to the Commissioner for Patents, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below.

Peggy Bailey

Date: March 1, 2004

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